Quarterly Progress Report

N01-NS-1-2333

Restoration of Hand and Arm Function by Functional Neuromuscular Stimulation

Period covered: October 1, 2002 to December 31, 2002

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Contract abstract

The overall goal of this contract is to provide virtually all individuals with a cervical level spinal cord injury, regardless of injury level and extent, with the opportunity to gain additional useful function through the use of FNS and complementary surgical techniques. Specifically, we will expand our applications to include individuals with high tetraplegia (C1-C4), low tetraplegia (C7), and incomplete injuries. We will also extend and enhance the performance provided to the existing C5-C6 group by using improved electrode technology for some muscles and by combining several upper extremity functions into a single neuroprosthesis. The new technologies that we will develop and implement in this proposal are: the use of nerve cuffs for complete activation in high tetraplegia, the use of current steering in nerve cuffs, imaging-based assessment of maximum muscle forces, denervation, and volume activated by electrodes, multiple DOF control, the use of dual implants, new neurotization surgeries for the reversal of denervation, new muscle transfer surgeries for high tetraplegia, and an improved forward dynamic model of the shoulder and elbow. During this contract period, all proposed neuroprostheses will come to fruition as clinically deployed and fully evaluated demonstrations.

Summary of activities during this reporting period

The following activities are described in this report:

- *Measurement of human upper extremity nerve diameters and branch-free lengths.*
- *Forward-dynamic shoulder and elbow model.*
- *Wireless data acquisition module for use with a neuroprosthesis.*
- *Preparation for percutaneous implementation of a hand grasp neuroprosthesis controlled by myoelectric signals from the wrist flexor and extensor.*

Measurement of human upper extremity nerve diameters and branch-free lengths.

Contract sections:
E.1.a.i Achieving Complete and Selective Activation Via Nerve Cuff Electrodes
E.2.a.i Selective Activation of Elbow and Shoulder Muscles by Nerve Cuff Electrodes

Introduction

The ability to activate selectively peripheral nerve trunk fascicles using nerve cuff electrodes is well established, and we will apply cuff electrodes to activate human upper extremity motor nerves. Studies of the external and internal topography of the targeted upper extremity nerves are necessary to identify suitable implant sites. The external study was previously reported and included measurements of the diameters and branch free lengths of the target nerves in six complete brachial plexus dissections. The results of this study indicated that diameters and branch free lengths of the targeted nerves are suitable for implantation of cuff electrodes. The goal of the internal study is to obtain accurate maps of the fascicular topography of the targeted nerves. These data will enable assessment of the suitability of the nerve topography for selective stimulation and enable implementation of anatomically accurate computer models of the targeted nerves. We are currently investigating the use of fluorescent

lipophilic dyes that diffuse in fixed nerve tissue and may enable retrograde tracing of peripheral nerve fascicles. In this quarter we focused on the application of DC electric fields to enhance the diffusion rates of the dyes.

Summary of Work This Quarter

Traditional cross-sectioning is largely ineffective as a means to follow fascicles through the length of a compound nerve. Figure 1 shows the significant degree to which peripheral nerve topography changes over relatively short distances and illustrates the difficult in identifying the same fascicle from cross-section to cross-section. Furthermore, traditionally cross-sectioning reveals no information about the location of functional groups at a sub-fascicular level.

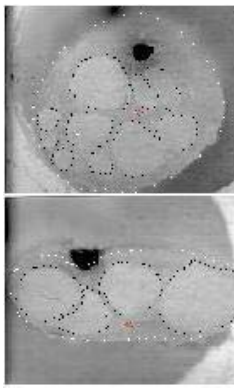

Figure 1. Radial nerve cross-sections 4mm apart.

Retrograde tracing utilizing lipophilic dyes has been used in postmortem formaldehyde fixed nerve fibers, but the maximal tracing distance has been limited by the slow diffusion rate that is seen in fixed tissue. For example, Lukas, et al., found a maximal tracing distance for DiI (1,1'-dioctadecyl-3,3,3'3'-tetramethlylindocarbocyanine perchlorate) of 29 mm, and for DiO (3,3'-dioctadecyloxa-carbocyanine perchlorate), and DiA (4-(4-dihexadecylamino)styryl)-*n*-methylpyridinium iodide) of 15-20 mm in fixed human tissue after incubation at 37 °C for 12-15 weeks. These distances are less than the 200 mm necessary to identify the location of muscle branches back to the targeted cuff electrode implantation sites.

The use of electric fields to enhance the diffusion of these three dyes (DiI, DiO, and DiA), as well as an additional analog (DiR), relies on the fact that they are all positively charged molecules. Thus, application of electric fields across the dye loaded nerve tissue should result in a force on the dye and enhanced diffusion. This hypothesis has been born out in our initial experiments.

A series of fixed human nerve samples were wrapped at either end with platinum wire electrodes. A triangular cross-section was then made in the nerve tissue approximately 1 cm from the anodic electrode and this cross-section was loaded with DiI. Electric fields ranging from 30-50 V/cm were applied across the loaded tissue for periods ranging from 48-130 hours.

Two of these trials had the initial loading site positioned within 20 mm of the cathodic electrode. After 96 hours of field application, both of these nerves exhibited extensive DiI accumulation at the location of the cathodic electrode. This DiI accumulation confirmed the field-enhanced diffusion of DiI. In an additional trial, the DiI loading site was positioned 1 cm from the anodic electrode in a 15 cm long nerve sample. Application of an electric field of 30 V/cm for 130 hours resulted in diffusion of DiI at least 89 mm from the initial loading site. This represented a 67 fold increase in diffusion velocity and a 3 fold increase in maximal tracing distance over the previously reported values. The results of these experiments illustrate that applied electric fields can enhance the diffusion rate and the maximum diffusion distance of lipophilic dyes. Field-enhanced diffusion is a method that has the potential to overcome the diffusion rate limitations of the lipophilic dyes in fixed tissue and enable retrograde tracing of individual nerve branches into compound nerve trunks.

Goals for Next Quarter

We will continue investigation of the field-enhanced diffusion of lipophilic dyes. Specifically we will quantify the relationship between the strength of the electric field, the tracing time, and the diffusion velocity of DiI. Tests of electric field enhanced diffusion of the other analogous dyes (DiO, DiA, and DiR) will also be conducted.

Forward-Dynamic Shoulder and Elbow Model

***Contract section**:*

E.1.a.ii.4.3 Development of a forward dynamic model of the human arm

Introduction

The musculoskeletal model of the shoulder and the elbow that has been used until now was developed by a group at the Technical University of Delft, headed by Dr. Frans van der Helm. It is a finite element model that includes 31 muscles and is used for inverse simulations, which means that the input is a particular mechanical state of the arm and the outputs are the muscle forces that are needed to achieve this state, specified by an optimization criterion. Inverse simulations are very useful for evaluating potential interventions in patients with tetraplegia (such as muscle transfers), or specifying muscle sets to provide certain functions when they are electrically stimulated. However, in order to develop an FNS controller for the arm, a forward model is needed, i.e., a model whose inputs are the muscle activations and outputs are the resulting forces and movements. This is necessary because the muscle stimulation parameters computed by the controller will vary with time, and the effects of these parameters need to be known so that the controller can have the proper effect.

Methods

In order to avoid the inconvenience of having two separate models for inverse and forward simulations, an overall dynamic musculoskeletal model is being developed using a set of commercially available software packages. SIMM (Software for Interactive Musculoskeletal Modeling, Musculographics, Inc.) is a graphics-based software system that allows users to develop, analyze, and visualize musculoskeletal models. The inputs to SIMM are a set of files that describe the joints, the muscles and the bones. The outputs are two software files in the C programming language; one containing information on muscle force generation and the other containing the description of the model needed for generating the equations of motion. This file is then used by SD/FAST, a separate software system available from Symbolic Dynamics, Inc. to compute the equations of motion. The Dynamics Pipeline is a suite of software subroutines available from Musculographics, Inc. that connects SIMM to SD/FAST in order to run forward and inverse simulations.

SIMM has been used in the past for lower extremity models, but the difficulties presented by the scapulo-thoracic gliding plane and the complex wrapping of certain arm muscles have made it impossible to use in the upper extremity. However, these problems have been solved in version 3.2 with the introduction of new wrapping objects, generalized coordinates and constraints. In order to make full use of these potentials, the president of Musculographics, Inc.

and main developer of SIMM provided a one-week training course on the new features of SIMM.

Results

The next step was the development of the input SIMM files, i.e. the muscle, joint and bone files. The muscle file contains the geometry (i.e. a series of attachment points) and the force-generating properties (i.e. peak isometric muscle force, optimal muscle-fiber length, pennation angle, tendon slack length, active and passive force-length relations and force-length relation) of the muscles. The coordinate frames were chosen to follow the protocol proposed by the International Society of Biomechanics, the International Shoulder Group and Delft University. The original authors of the inverse dynamics model have developed experimental procedures to measure the muscle parameters from cadavers, so these parameters were transferred directly into the SIMM environment.

In the joint file, the body segments, joints, generalized coordinates, muscle wrap objects and kinematic functions are defined. The joints and wrap objects have already been implemented, but this file is not yet completed. Namely, the constraints on the generalized coordinates and the kinematic functions are currently being developed. The last set of files is the bone files, which contain lists of polygons defining the bone surfaces. A general model of the upper body skeleton is currently being used, but with the bone editor (which is a new feature of SIMM) the manipulation of these surfaces will be facilitated. Precision is not required when creating the bones, because they are merely visual aids for moving the joints and placing the muscles, and they are not necessary for developing and analyzing models in SIMM.

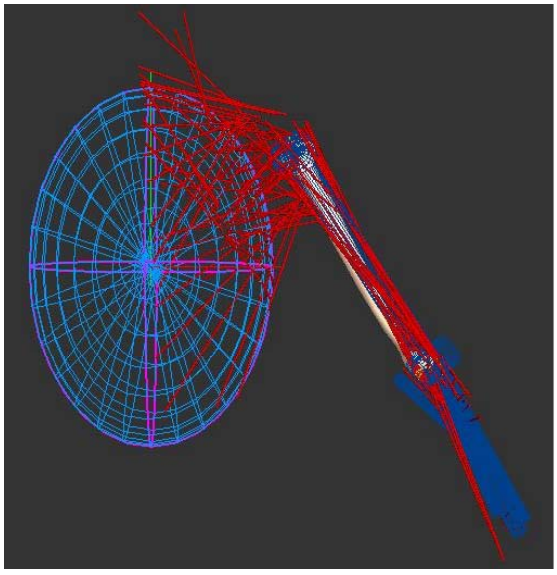

Figure 2. Posterior view of the model with 30 degrees of humerus elevation. The red lines are the muscles, the blue surfaces are the wrap objects and the humerus is included as an example of a bone structure.

Next Quarter

When the SIMM model is completed, it will be connected to SD/FAST through the Dynamics Pipeline to create forward and inverse simulation routines. It will be validated by running inverse simulations and comparing the results with those provided by the existing inverse-dynamic model. When its validity is determined, it will be used to perform forward simulations using different muscle activation patterns and external disturbances. This capability will be a useful tool for the development of FNS controllers.

Wireless Data Acquisition Module for Use with a Neuroprosthesis

***Contract section**:* E.1.a.v Sensory feedback of contact and grasp force

Abstract

The originally proposed plan of developing a thumbnail-mounted contact sensor that is connected to a small wireless transmitter has been altered so that now a general wireless data acquisition module is being developed. In addition to the thumbnail-mounted contact sensor, this general module could be utilized for other sensors used with a neuroprosthesis, such as the shoulder or wrist position transducer, finger-mounted joysticks, or remote on-off switches. Currently these sensors are connected to a controller via cables, which are cosmetically unappealing to the user and often get caught on wheelchairs, causing them to be damaged. Switch-activated transmitters mounted on walkers have been used previously in FES applications [1]. Recent advances in wireless technology have reduced the complexity and size of the wireless circuitry and have increased the likelihood that a small, low power, reliable wireless link could be assembled from commercially available components.

Methods

In the previous progress report, the successful transmission of sampled data from one transceiver module to another was described. Data packets included a start symbol, a packet number, device numbers and a sampled data value. These packets were encoded with a Manchester encoding scheme to provide a symmetrical signal to the receiver portion of the circuit.

In this quarter, a CRC error-checking algorithm was implemented on both the transmitting and receiving software. The transmitting software creates a 16-bit CRC value based on the contents of the data packet. This CRC value is Manchester-encoded and appended to the data packet, adding four bytes to the length of the data packet. After sending its data packet, the transmitting software waits for a reply packet.

The receiving software repeats the CRC algorithm on the portion of the data packet prior to the transmitted CRC value and compares the two values. If the two values match, a reply packet is prepared, consisting of a start symbol, the packet number, and the device numbers, forming a three-byte packet. If the two CRC values do not match, a one is added to an unused bit in the packet number byte, indicating a CRC error. The reply packet is then assembled as described above. The reply packet is transmitted and the receiving software returns to listening for a data packet.

When the transmitting software detects a reply packet, it checks the device numbers in the packet. If the device numbers are correct, it checks the packet number. If the packet number is correct, the message is considered to be acknowledged. If the packet number is altered so that it has a one in the unused bit position, then it is considered to be a CRC error. If there is an incorrect device number, incorrect packet number, CRC error, or if no reply packet is detected in the allotted time, the original data packet is re-sent. If two attempts to re-send the data packet are unsuccessful, the transmitting software continues on with the next data packet.

Results

Message Accuracy

When the error-checking and reply packet software was completed, a test was performed to determine how many data packet messages were transmitted successfully. Ten thousand data packet messages were sent. Of these 10,000 messages, 75 needed to be re-transmitted. Forty-three of the re-transmitted messages were due to CRC errors; 30 were due to address errors; 1 was due to an incorrect packet number; and 1 packet contained no data. After re-transmission, all 75 packets were received properly. Thus 99.25% of the messages were transmitted properly on the first attempt, and 100% were transmitted properly when re-transmission attempts were included. An example of the data packet and reply packet are shown in Figure 1.

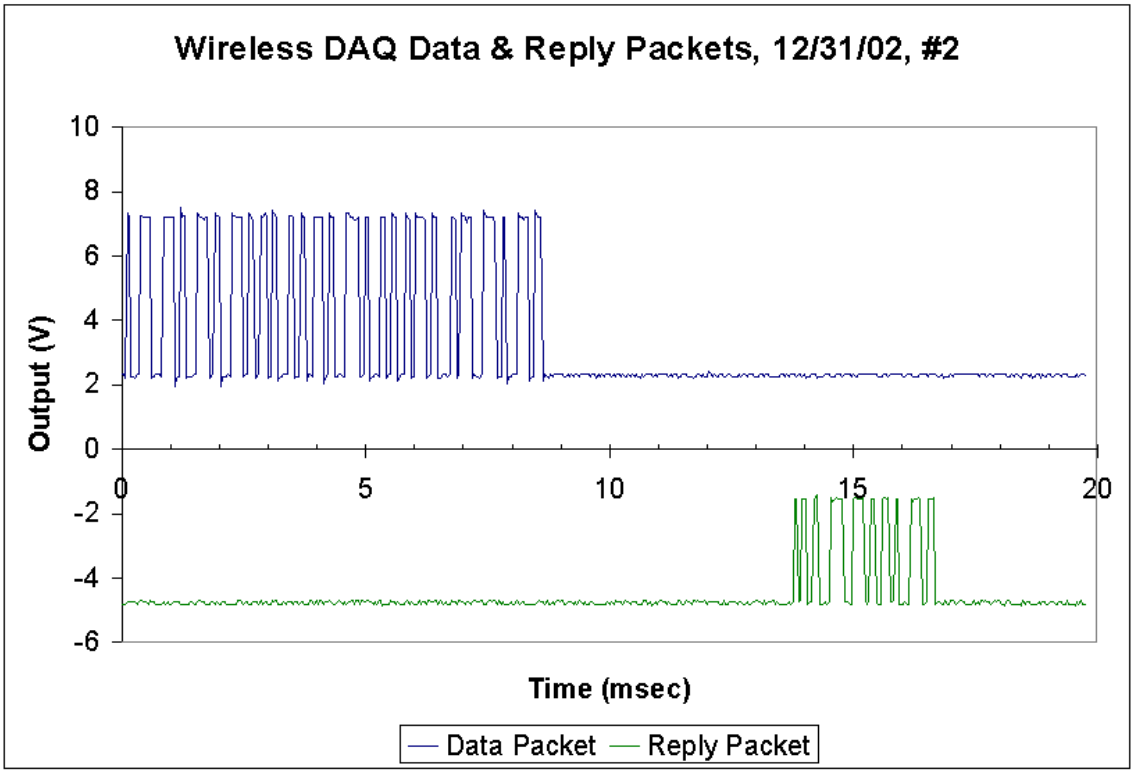

Figure 3. Data and reply packets.

Data Rate

Currently, the data packet requires approximately 9 msec to send 9 bytes of data (packet number, device addresses, data value, CRC value). The reply packet requires approximately 3 msec to send 3 bytes (packet number, device addresses). The data and reply packet combination requires approximately 17 msec to complete (see Figure 1), allowing a maximum data rate of 59 Hz. The software is currently set for a data rate of 20 Hz. Increases in the maximum data rate will be pursued in the future by using more sophisticated software timing techniques, thus allowing a reduction in the minimum pulse width for the data packets.

Current Requirements

The average current utilized by the transceiver circuits was measured with a multimeter during data transmission. The circuits used 25.7 – 32.1 mA. The transceiver boards are prototypes that have components that are included for test purposes only. One component is a potentiometer that draws 5 mA. Another is a voltage regulator that draws 10.3 mA. If these items were eliminated, the transceiver circuit would draw 10.4 – 16.8 mA.

The current draw variation was investigated by measuring the voltage across a 10 ohm resistor placed in series with the battery. An example of this current variation is shown in Figure 2. The current draw peaks during the data packet transmission, then reduces by a few milliamps during the reply packet transmission, after which it reduces to a stable level between transmissions.

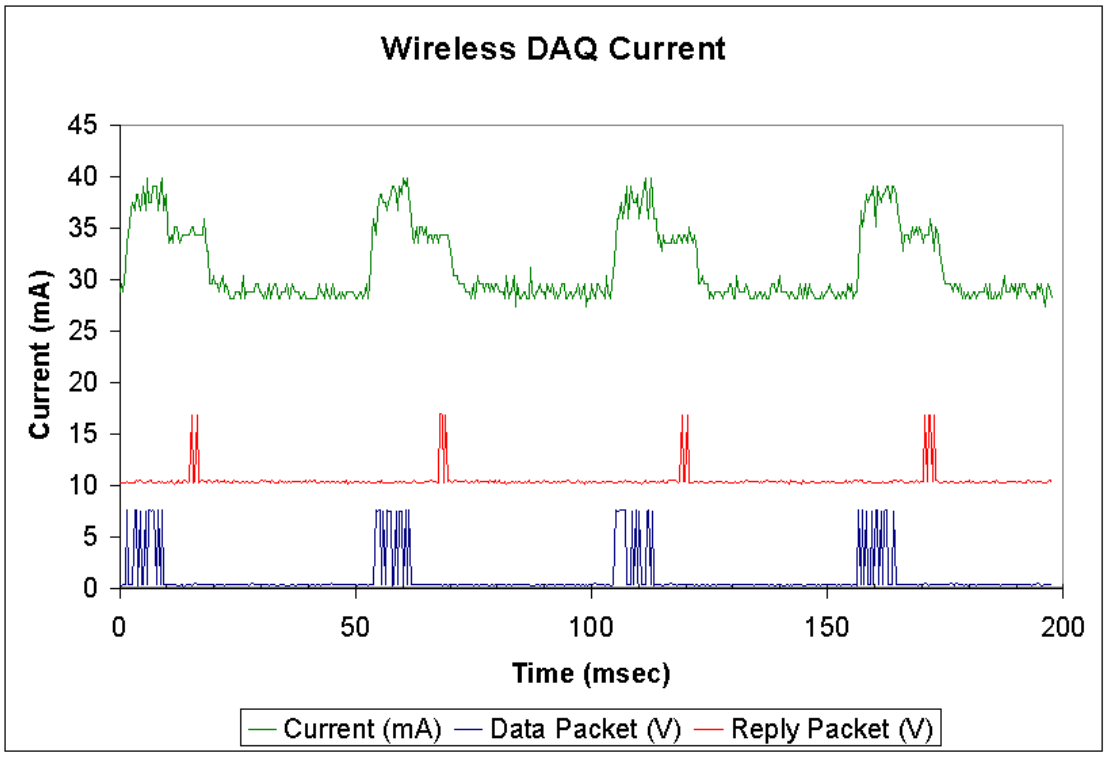

Figure 4. Current variation for wireless module.

Next quarter

The present hardware utilizes an RF transceiver development board connected to a microcontroller development board. In the next quarter, a prototype microcontroller board will be designed and built. This board will be smaller in size than the development board, and will eliminate the extraneous circuitry of the development board. This microcontroller board will be connected to an already-purchased RF transceiver module that is smaller than the RF transceiver development board. This microcontroller & transceiver prototype will allow a better evaluation of the power requirements and packaging requirements for the wireless data acquisition module. It will also allow us to evaluate different antenna configurations.

Also in the next quarter, a review will be made of the available battery options for the wireless data acquisition module.

References

[1] Z. Matjacic, M. Munih, T. Bajd, A. Kralj, H. Benko, and P. Obreza, "Wireless control of functional electrical stimulation systems," *Artif Organs*, vol. 21, pp. 197-200, 1997.

Preparation for Percutaneous Implementation of a Hand Grasp Neuroprosthesis Controlled by Myoelectric Signals from the Wrist Flexor and Extensor

Contract section: E.1.b Control of Grasp Release in Lower Level Tetraplegia

Abstract

The purpose of this research is to develop and evaluate an advanced neuroprosthesis to restore hand function in persons with OCu:5 and OCu:6 (International classification) spinal cord injuries. Through this work we will implement in human subjects a control methodology utilizing myoelectric signals (MES) from muscles synergistic to hand function to govern the activation of paralyzed, electrically stimulatable muscles of the forearm and hand. This work encompasses the following objectives:

1) Characterize the myoelectric signals (MES) recorded from a pair of muscles synergistic to hand function, demonstrating that the signals are suitable for neuroprosthesis control
2) Demonstrate the ability of subjects to use the proposed control algorithm to control a simulated neuroprosthesis
3) Implement myoelectric control of the hand grasp neuroprosthesis in subjects with C7 level spinal cord injury and evaluate hand performance

Progress Report

During this quarter, MES characterization and control simulation studies were conducted with a second subject with C7 spinal cord injury. Also preparations were made for percutaneous implementation of myoelectric-controlled electrical stimulation of hand grasp (objective 3).

MES Characterization and Control Simulation Studies

Subject 8 was a 36 year old male with grade 4 wrist flexion and grade 5 wrist extension in the side that was tested (right). He retained little voluntary finger and thumb flexion (grade 1 or less) and grade 3+ finger extension. Prior to these experiments, he was evaluated for FES intervention, and it was found that the finger flexors did not respond to electrical stimulation, suggesting denervation of those muscles. Fine-wire EMG recording electrodes (Nicolet Biomedical, Inc.) were implanted into the wrist flexor (flexor carpi radialis - FCR) and extensor (extensor carpi radialis brevis/longus - ECR).

We recorded MES from the wrist flexor and extensor during trials in which the subject was instructed to a) relax the wrist muscles, b) flex the wrist with a range of contraction strengths, and c) extend the wrist with a range of contraction strengths. Data from these trials

were displayed on a graph of signal space (ECR MES versus FCR MES). The data collected during wrist flexion (o) and extension (+) occupied distinct regions of signal space (Figure 5). Boundaries were established to partition the signal space into regions corresponding to distinct neuroprosthesis states. It is the definition of these regions that customizes the control algorithm. The control algorithm maps each point of signal space to a particular neuroprosthesis state -- Close, Open, Hold, or Change Grasp Pattern. The boundaries are placed so that the region of signal space corresponding to wrist extension maps to the Open state; the wrist flexion region maps to the Close state; the wrist relaxed region maps to the Hold state, and a strong co-contraction maps to Change Grasp Pattern. For this subject, the boundaries were positioned so that significant shifts in the data during wrist flexion and extension would be accommodated by the control algorithm.

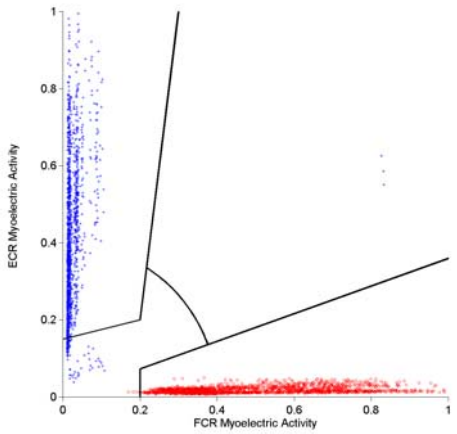

Figure 5. Wrist flexion (o) and extension (+) data from SCI subject. The data occupy distinct regions of signal space. Ample margin for data shifts has been given in placing the boundaries that define NP states.

The control algorithm was used to govern the opening and closing of a virtual hand presented on a computer screen. The virtual hand appeared as a 'Pac-man' like figure that opened and closed in response to the myoelectric activity of the wrist muscles. The subject controlled the motion of the virtual hand by selecting appropriate neuroprosthesis states by flexing, extending, or relaxing his wrist muscles. A test was conducted to evaluate the ability of the subject to control the degree of opening and closing of the virtual hand. A target hand position was superimposed on the virtual hand and the subject's task was to move the virtual hand so that it matched the target position within +/-5%. The rate of success in matching the target positions and the incidence and magnitude of error were recorded. An error was registered whenever the MES-controlled virtual hand position moved away from instead of toward the target hand position. Such errors occurred when the target position was overshot or when the subject activated the open state when the close state should have been activated or vice versa.

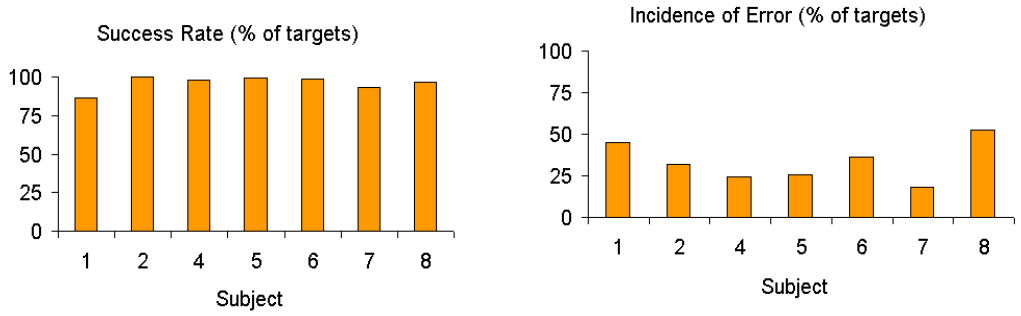

Figure 6. Subject 8 showed high proficiency in matching target hand positions, but had a high incidence of error.

The subject's performance in controlling the position of the virtual hand was compared to that of the subjects previously tested (Figure 6). Subject 8 matched 97% of the target

presentations; the range of success rates across all subjects was 87% to 100%. Subject 8 made one or more errors during 53% of the target presentations; the range of incidence of error ranged from 18% to 53% across all subjects. Subject 8 had the largest incidence of error of all the subjects tested so far. The reason subject 8 had a large incidence of error was because he often attempted to correct even inconsequential overshoots or undershoots (within +/- 5%) of the target position. These attempts at minute corrections often led to an overshoot beyond 5% of the target position resulting in registration of an error.

Perhaps the most relevant outcome measure is the magnitude of errors that were made, and whether the magnitude is large enough to result in a significant inadvertent alteration of hand position or grip during actual use of the hand grasp system. Figure 7 shows the distribution of errors committed that resulted in various magnitudes of command signal change. Most of the errors resulted in small changes in command signal. For subject 8, 84% of his errors resulted in inadvertent changes of command signal of less than 15%. For all subjects combined, 90% of the errors committed resulted in inadvertent changes in command signal of less than 15%. Therefore, most of the errors resulted in changes in command signal that are not expected to correspond to significant changes in hand position or force.

Preparations for Percutaneous Implementation

The third objective of this contract section is to implement myoelectric control of hand grasp in C7 subjects. We will test this implementation percutaneously before proceeding to fully implanted system implementations. The percutaneous implementation protocol will require three to four weeks of subject participation. During the first week, we will implant percutaneous intramuscular electrodes for EMG recording and for electrical stimulation. The stimulation electrodes (Knutson, et al. 2002) will be implanted into key finger and thumb muscles required for producing strong hand grasp and release. The recording electrodes will be implanted in the wrist flexor and extensor muscles. We will conduct EMG characterization studies and design

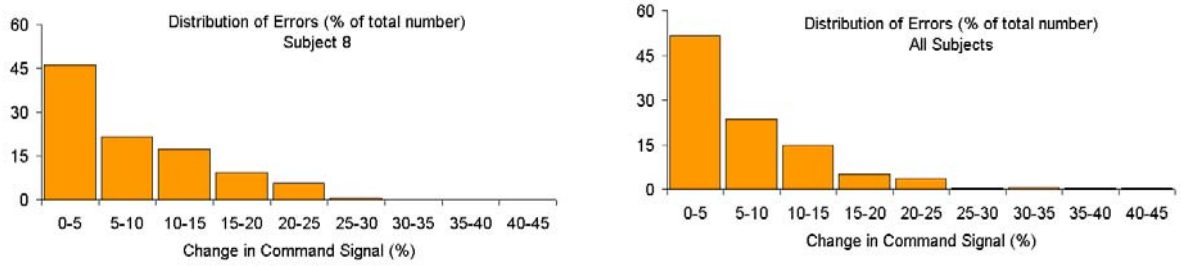

Figure 7. The distribution of errors committed by subject 8 is similar to the pooled distribution of errors across all subjects. Most errors result in small inadvertent alterations in command signal.

and test the control algorithm during the second week. During the third and fourth weeks, we will evaluate the subjects' ability to open and close their hands with myoelectric control of electrical stimulation. We will evaluate pinch strength, range of motion, performance in the grasp release test (Stroh-Wuolle, et al. 1994), and performance in hand function. These measures of hand impairment and function will be compared to that achieved using a wrist position sensor to control the hand (Hart, et al. 1998).

The electrodes we will use for EMG recording will be of the design described by Mortimer and Yodlowski (1979). These electrodes are expected to be of adequate durability to withstand 3 to 4 weeks in the body. During this quarter, we completed fabrication of a small supply of these electrodes (Figure 8). The electrodes were fabricated from two 46 μm diameter stainless steel wires coiled around a 7-mil arbor, producing an electrode with an outer diameter of 0.38 mm. A 22-gauge needle will be used to implant these electrodes. The spacing between the two deinsulated sections of the electrode influences the characteristics of the recorded EMG signal. We have fabricated electrodes with a spacing of 1 mm to 4 mm, and will perform a pilot test to determine which spacing gives the best signal-to-noise characteristics.

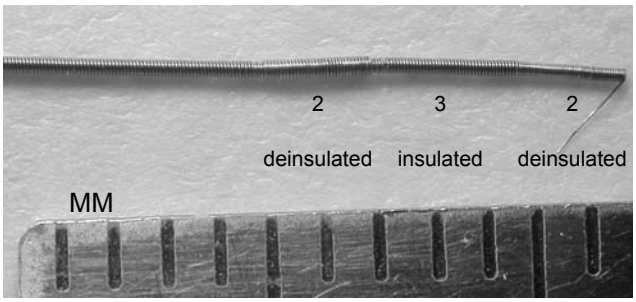

Figure 8. EMG recording electrode to be used in percutaneous implementation of myoelectric control of electrical stimulation.

Figure 9 shows how the electrodes will be interfaced to equipment in the laboratory. The stimulating electrodes will be interfaced with an external stimulator, which will output electrical pulses in accordance with a command signal generated from the myoelectric control algorithm. The stimulator will also generate a trigger pulse 2 msec prior to each cycle of stimulation pulses. The trigger pulse will be sent to the EMG amplifier and data acquisition board and will be used to blank the EMG signal and remove data during the expected stimulation artifact.

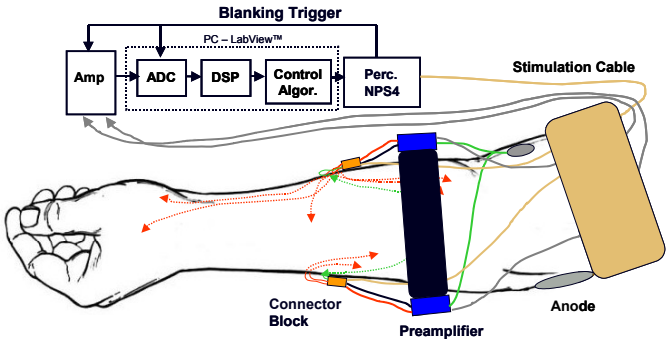

Figure 9. Lab setup for evaluating myoelectric control of electrically stimulated hand grasp in individuals with C7 tetraplegia.

During this quarter, the LabView routine that controls data acquisition was modified. Code was added for removing stimulation artifact and for communicating with the stimulator. Preliminary testing of the setup has begun.

Next Quarter

A pilot test will be done to assess the EMG recording capabilities of the electrodes we have fabricated and to decide what bipolar spacing to use in subsequent subjects. The pilot test will include testing of the percutaneous setup to ensure that adequate artifact blanking is possible and that the response time of the system is acceptable. Individuals with C7 SCI will be recruited to participate in the percutaneous study.

References

Hart RL, Kilgore KL, Peckham PH. A comparison between control methods for implanted FES hand-grasp systems. IEEE Trans Rehabil Eng 6:208-218, 1998.

Knutson JS, Naples GG, Peckham PH, Keith MW. Electrode fracture rates and occurrences of infection and granuloma associated with percutaneous intramuscular electrodes in upper-limb functional electrical stimulation applications. J Rehabil Res Dev 39:671-684, 2002.

Mortimer JT, Yodlowski EH. Frequency sweep analysis of neuromuscular junction continuity. J Med Eng Technol 3:242-247, 1979.

Stroh-Wuolle K, VanDoren CL, Thrope GB, Keith MW, Peckham PH. Development of a quantitative hand grasp and release test for patients with tetraplegia using a hand neuroprosthesis. J Hand Surg 19A:209-218, 1994.